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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/899,412 | 07/05/2001 | Neal R. Cutler | CUTLER-06326 | 3297 |

23535 7590 05/20/2005

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| EXAMINER | |
|---|---|
| YEBASSA, DESTA LETTA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1615 | |

DATE MAILED: 05/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/899,412 | CUTLER, NEAL R. | |
| | Examiner | Art Unit | |
| | Desta L. Yebassa | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8,13, and 16- 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,13,and 16- 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



RD

## DETAILED ACTION

Receipt is acknowledged of applicant's Amendment and Responses filed on 03/11/2005.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 2, 4-8 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caruso (US 6043244).

Caruso teaches a method treating migraines wherein dihydroergotamine is administered with an antimigraine-potentiating amount of an NMDA receptor antagonist (Col. 3, lines 14-58). Caruso contemplates all modes of administration (Col. 6, lines 3-67', Col. 7, lines 1-31). Specifically, sublingual administration is taught in the form of a tablet, drop or lozenge (Col. 6, lines 25-28). Sprays, pastes or gels are also taught by Caruso (Col. 6, lines 30-35, 63-65). The oral

tablets further comprise additives such as calcium carbonate, calcium phosphate or kaolin (Col. 6, lines 18-24). Additional active agents may be added to the composition (Col. 8, lines ,12-27). Caruso recites DHE and its pharmaceutically acceptable salts (Col. 3, lines 14-40). It is the position of the Examiner that any form of DHE, the salt or the base would be acceptable for the formulation of Caruso.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to formulate a sublingual composition that contains DHE and a pH-adjusting agent. Elimination of an ingredient as well as its function does not impart patentability to a well-known formulation in the absence of said ingredient.

One of ordinary skill in the art would have been motivated to do this to provide a method of treating migraines that is effective and achieves the effect in a short amount of time to bring quick and direct relief to the host.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 4-8 and 13 are rejected under 35 U.S.C. 1O3(a) as being unpatentable over Plachetka (U.S Patent No. 5872145).

Plachetka teaches a method of treating migraines wherein an effective amount of a 5-HT agonist and NSAID are administered to a patient (Col. 13, Claim 1', Col. 3, lines 64-67). The 5-HT agonists include all types of 5-HT agonists, more specifically, 5-HT1, 5-HT1 B and 5-HT1 D agonists (Col. 8, lines 1-20). Dihydroergotamine mesylate is one such example (Col. 8, lines 1-20). The combination of active agents can be

administered parenterally, enterally and topically and can be administered with appropriate carrier as well as other pharmaceutically acceptable excipients (Col. 12, line 31 - Col. 13, line 19). The dosage form can be in the form of quick-dissolve tablet (Col. 13, Claim 17).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to formulate a sublingual composition that contains DHE and a pH-adjusting agent. Elimination of an ingredient as well as its function does not impart patentability to a well-known formulation in the absence of said ingredient.

One of ordinary skill in the art would have been motivated to do this to provide a method of treating migraines that is effective and achieves the effect in a short amount of time to bring quick and direct relief to the host.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Caruso or Plachetka in combination with Azria et al. (US 4758423) or Plachetka et al. (US 6495535, hereinafter '535). The teachings of Caruso and Plachetka are discussed above. Neither reference teaches that the DHE is in the base form. It is the position of the Examiner that any form of DHE would be effective in treating migraines. No criticality is seen in DHE being in the form of a base. Applicants have not shown any unexpected results from the base form. Further, the secondary references teach that the base form of DHE is known to be administered for treating migraines (Azria, Col. 3, lines 32-39', Plachetka, Col. 4, lines 1-4).

Claims 16 and 17 are rejected under 35 U.S.C. 1O3(a) as being unpatentable over Peyman (U.S Patent No. 5855907).

Peyman teaches a method of treatment with an anti-inflammatory compound, which is a steroid; preferably, the steroid is gluocorticoid (column 2, lines 55). A method of treatment of migraine comprising the topical administration of an opioid with combination of anti-inflammatory compounds include steroids, particularly glucocorticoids, for example, cortisol, cortisone, prednisolone, dexamethasone and the like (column 5, line 55-65).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use any form of DHE is a method of treating migraines, including the base form.

One of ordinary skill in the art would have been motivated to do this to provide a method treating migraines that is effective and achieves the elect in a short amount of time to bring quick and direct relief to the host.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

**Response to Arguments**

Applicant argue that the prior art does not teach PH modulating agent, failure to make a prima facie case of obviousness and the examiner has provided nothing but bald, perfunctory, conclusory statements. The applicant furthermore, argued that the reference does not teach co-formulation of a steroid.

Applicant's arguments filed 03/11/2005 have been fully considered but they are not persuasive.

The Examiner would like to point out that all combinations of references teach ingredients/components of the formulations that modulate the pH of the environment in which they are placed. Caruso teaches that components such as calcium carbonate can be used (Col. 6, lines 18-24). Further, Caruso is used to teach that DHE is a known antimigraine agent and can be administered in the form of a tablet formulated in any conventional manner to the oral mucosa for buccal and/or sublingual administration (Col. 6, lines 25-28). Plachetka teaches that DHE can be administered with appropriate carrier as well as other pharmaceutically acceptable excipients, including buffers, which can be modulating PH (Col. 12, line 31 - Col. 13, line 19). Peyman teaches a method of treatment with an anti-inflammatory compound, which is a steroid; preferably, the steroid is gluocorticoid ( column 2, lines 55). A method of treatment of migraine comprising the topical administration of an opioid with combination of anti-inflammatory compounds include steroids, particularly glucocorticoids, for example, cortisol, cortisone, prednisolone, dexamethasone and the like (column 5, line 55-65). Therefore, applicants' arguments are found unpersuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. The Examiner is not making mere bald, perfunctory, conclusory

accusations to formulate the instant rejection. The Examiner is using only the knowledge of the combinations of the references cited above.

It is the position of the Examiner that the combinations of the prior art references are proper and the references recited teach the Imitations of the instant claims. Therefore, for the reasons stated above, applicant's arguments are unpersuasive and the prior art rejections are maintained.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

## Telephonic Inquiry

Any inquiry concerning this communication from the examiner should be directed to Examiner Desta L Yebassa whose telephone number is (571) 272-8511. The examiner can normally be reached on Mon.-Friday 8:00 - 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

Supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone Number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600